

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims:

Claims 1 – 120. (Canceled)

121. (Currently amended) An antibody, or antigen-binding fragment thereof, which is a variant of monoclonal antibody HUIV26 having one or more complementarity determining regions (CDRs) having an amino acid sequence differing from the corresponding CDRs of monoclonal antibody HUIV26, and which has higher binding affinity for denatured collagen type IV over native collagen type IV comprising a heavy chain variable region and a light chain variable region, wherein ~~at least one of the CDRs in the heavy chain variable region or the light chain variable region comprises one or more substitutions selected from said heavy chain variable region~~ comprises:

- (i) a heavy chain CDR1 having the amino acid sequence of SEQ ID NO: 26 or the amino acid sequence of SEQ ID NO: 26 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of arginine at position 6 therein by histidine;
 - (b) substitution of methionine at position 9 therein by isoleucine; and
 - (c) substitution of serine at position 10 therein by threonine, alanine or glycine; ~~and~~
- (ii) a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 28 or the amino acid sequence of SEQ ID NO: 28 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of isoleucine at position 9 therein by alanine, serine or valine;
 - (b) substitution of serine at position 14 therein by tyrosine, alanine, histidine or glycine;
 - (c) substitution of lysine at position 16 therein by aspartic acid or glutamine; and

- (d) substitution of aspartic acid at position 17 therein by lysine or serine;
and
- (iii) a more heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 30 or the amino acid sequence of SEQ ID NO: 30 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of aspartic acid at position 3 therein by proline, glycine, threonine or alanine;
 - (b) substitution of glycine at position 4 therein by proline, alanine or histidine; and
 - (c) substitution of tyrosine at position 11 therein by proline or asparagine;
and

wherein said light chain variable region comprises:

- (iv) a light chain CDR1 having the amino acid sequence of SEQ ID NO: 20 or the amino acid sequence of SEQ ID NO: 20 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of glutamine at position 4 therein by arginine or serine;
 - (b) substitution of asparagine at position 8 therein by serine;
 - (c) substitution of serine at position 9 therein by tyrosine, tryptophan, histidine or arginine;
 - (d) substitution of glycine at position 10 therein by tyrosine, arginine, histidine or isoleucine; and
 - (e) substitution of glutamine at position 12 therein by lysine; and
- (v) a light chain CDR2 having the amino acid sequence of SEQ ID NO: 22; and
- (vi) a light chain CDR3 having the amino acid sequence of SEQ ID NO: 24 or the amino acid sequence of SEQ ID NO: 24 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of serine at position 5 therein by glutamine, glycine, leucine, alanine, threonine or valine; and

- (b) substitution of tyrosine at position 6 therein by asparagine, serine, proline or methionine.

122. **(Previously presented)** The antibody or antigen-binding fragment thereof, of claim 121, wherein said heavy chain CDRs are grafted into a VHIII/JH6 heavy chain variable region framework referenced as SEQ ID NO: 8.

123. **(Previously presented)** The antigen-binding fragment of claim 121, wherein said antigen binding fragment is selected from Fv, Fab, F(ab)₂ and scFV fragments.

124. **(Currently amended)** The antibody or antigen-binding fragment thereof, of claim 121, comprising two of any of said substitutions in the CDRs.

125. **(Currently amended)** The antibody or antigen-binding fragment thereof, of claim 121, comprising three of any of said substitutions in the CDRs.

126. **(Currently amended)** The antibody or antigen-binding fragment thereof, of claim 121, comprising four of any of said substitutions in the CDRs.

127. **(Currently amended)** The antibody or antigen-binding fragment thereof, of claim 121, comprising five or more of any of said substitutions in the CDRs.

128. **(Previously presented)** A nucleic acid encoding an antibody, or antigen binding fragment thereof, of claim 121.

129. **(Previously presented)** The antibody or antigen binding fragment thereof of claim 121, wherein said antibody, or antigen binding fragment thereof, further comprises a therapeutic moiety.

130. **(Previously presented)** The antibody or antigen binding fragment thereof of claim 121, wherein said antibody, or antigen binding fragment thereof, further comprises a diagnostic moiety.

131. **(Currently amended)** A grafted antibody, or antigen-binding fragment thereof, which is a variant of monoclonal antibody HUIV26 having one or more complementarity determining regions (CDRs) having an amino acid sequence differing from the corresponding CDRs of monoclonal antibody HUIV26, and which has higher binding affinity for denatured collagen type IV over native collagen type IV comprising a heavy chain variable region and a light chain variable region, wherein at least one of the CDRs in the heavy chain variable region or the light chain

~~variable region comprises one or more substitutions selected from~~ said heavy chain variable region comprises:

- (i) a heavy chain CDR1 having the amino acid sequence of SEQ ID NO: 26 or the amino acid sequence of SEQ ID NO: 26 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of arginine at position 6 therein by histidine;
 - (b) substitution of methionine at position 9 therein by isoleucine; and
 - (c) substitution of serine at position 10 therein by threonine, alanine or glycine; and
- (ii) a heavy chain CDR2 having the amino acid sequence of SEQ ID NO: 28 or the amino acid sequence of SEQ ID NO: 28 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of isoleucine at position 9 therein by alanine, serine or valine;
 - (b) substitution of serine at position 14 therein by tyrosine, alanine, histidine or glycine;
 - (c) substitution of lysine at position 16 therein by aspartic acid or glutamine; and
 - (d) substitution of aspartic acid at position 17 therein by lysine or serine; and
- (iii) a heavy chain CDR3 having the amino acid sequence of SEQ ID NO: 30 or the amino acid sequence of SEQ ID NO: 30 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of aspartic acid at position 3 therein by proline, glycine, threonine or alanine;
 - (b) substitution of glycine at position 4 therein by proline, alanine or histidine; and
 - (c) substitution of tyrosine at position 11 therein by proline or asparagine; and

wherein said light chain variable region comprises:

- (iv) a light chain CDR1 having the amino acid sequence of SEQ ID NO: 20 or the amino acid sequence of SEQ ID NO: 20 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of glutamine at position 4 therein by arginine or serine;
 - (b) substitution of asparagine at position 8 therein by serine;
 - (c) substitution of serine at position 9 therein by tyrosine, tryptophan, histidine or arginine;
 - (d) substitution of glycine at position 10 therein by tyrosine, arginine, histidine or isoleucine; and
 - (e) substitution of glutamine at position 12 therein by lysine; and
- (v) a light chain CDR2 having the amino acid sequence of SEQ ID NO: 22; and
- (vi) a light chain CDR3 having the amino acid sequence of SEQ ID NO: 24 or the amino acid sequence of SEQ ID NO: 24 but for having one or more substitutions selected from the group consisting of:
 - (a) substitution of serine at position 5 therein by glutamine, glycine, leucine, alanine, threonine or valine; and
 - (b) substitution of tyrosine at position 6 therein by asparagine, serine, proline or methionine.

132. **(Previously presented)** The grafted antibody or antigen-binding fragment thereof of claim 131, wherein the heavy chain CDRs are grafted into a VHIII/JH6 heavy chain variable region framework referenced as SEQ ID NO: 8.

133. **(Previously presented)** The antigen-binding fragment of claim 131, wherein said antigen binding fragment is selected from Fv, Fab, F(ab)₂ and scFV fragments.

134. **(Previously presented)** A nucleic acid encoding an antibody or antigen binding fragment thereof of claim 131.

135. **(Previously presented)** The grafted antibody or antigen binding fragment thereof of claim 131, wherein said grafted antibody, or antigen binding fragment thereof, further comprises a therapeutic moiety.

136. **(Previously presented)** The grafted antibody or antigen binding fragment thereof of claim 131, wherein said grafted antibody, or antigen binding fragment thereof, further comprises a diagnostic moiety.

137. **(Currently amended)** The grafted antibody or antigen-binding fragment thereof, of claim 131, comprising two of any of said substitutions in the CDRs.

138. **(Currently amended)** The grafted antibody or antigen-binding fragment thereof, of claim 131, comprising three of any of said substitutions in the CDRs.

139. **(Currently amended)** The grafted antibody or antigen-binding fragment thereof, of claim 131, comprising four of any of said substitutions in the CDRs.

140. **(Currently amended)** The grafted antibody or antigen-binding fragment thereof, of claim 131, comprising five or more of any of said substitutions in the CDRs.

141. **(Currently amended)** The antibody, or antigen-binding fragment thereof, of claim 121 wherein said antibody, or antigen-binding fragment thereof, comprises a heavy chain CDR1 referenced as SEQ ID NO:45; a heavy chain CDR2 referenced as SEQ ID NO:155; a heavy chain CDR3 referenced as SEQ ID NO:63; a light chain CDR1 referenced as SEQ ID NO:157; a light chain CDR2 referenced as SEQ ID NO:22; and a light chain CDR3 referenced as SEQ ID NO:77; ~~and which binds denatured collagen.~~

142-158. **(Canceled)**